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| APPLICANT: | Robert C. Leif, et al. | EXAMINER: | Perreira, Melissa Jean |
| SERIAL NO.: | 10/578,355 | ART UNIT: | 1618 |
| FILED: | June 12, 2006 | | |
| TITLE: | A REAGENT SYSTEM AND METHOD FOR MODIFYING THE LUMINESCENCE OF LANTHANIDE(III) MACROCYCLIC COMPLEXES | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DR. ROBERT C. LEIF

I, Robert C. Leif, hereby declare:

1. I received a B.S. in Biochemistry from the University of Chicago in 1959;
2. I received a Ph.D. in Chemistry from the California Institute of Technology in 1964;
3. I am currently Vice President and Research Director for Newport Instruments, San Diego, California;
4. I am listed as an inventor on 11 issued U.S. Patents;
5. I am an author on 102 scientific papers, 21 of which are related to lanthanide luminescence;
6. I have edited 17 books directed to scientific subject matter;
7. I am a listed inventor on U.S. Patent Application No. 10/578,355, which is the application at issue in the present case, and I make the present Declaration in support of that application based on personal knowledge;
8. I am a listed inventor on issued U.S. Patent No. 6,340,744 ("the '744 patent"), which has been cited against the present application;
9. The subject matter of the '744 patent is an aqueous micellar solution, whereas the claims of the present application, as amended herewith, are directed to a solid as well

as to a single-phase luminescence enhancing solution that dries to form a luminescence enhancing solid. This aspect of the present invention resulted from the unexpected discovery that a micelle-producing amount of at least one surfactant is not required for solid state luminescence.

10. The '744 patent also requires a yttrium or a 3-valent lanthanide element having atomic number 59-71. One aspect of the present invention resulted from the unexpected discovery that neither yttrium or a 3-valent lanthanide element having atomic number 59-71 is necessary for enhancing the solid state luminescence of the present invention.

11. The '744 patent teaches away from the present invention in column 10, lines 21 through 34, which read: "The enhanced luminescence composition of the ['744] invention exists in a micellar organization. The importance of micellar organization to the enhanced luminescence composition is demonstrated by the observation that a water-miscible polar solvent such as ethanol when added to the characteristically cloudy and luminous composition completely discharges the luminescence and simultaneously turns the cloudy micellar liquid clear. Once formed in an aqueous micellar organization the composition of the invention can be transferred to an immiscible non-aqueous medium and/or dried, as by evaporation or lyophilization, with preservation of its luminescence. To provide the micellar organization, the composition includes a micelle-forming amount of a surfactant;"

12. The micellar solutions of the '744 patent have a number of problems associated therewith, including limited stability, limited reproducibility of the micellar solutions, and the impairment of cellular morphology by the emulsifying agents. The compositions of the present invention overcome these problems while being easily transportable and remaining suitable for use in luminescence enhancing applications;


13. Figure 6 of Example X of the present application shows a surprising increase in the luminescence of a europium-streptavidin conjugate with the addition of TTFA, to reach a maximum of over one million HTTFA per europium macrocycle at a concentration of 3mM HTTFA. Since there was no gadolinium(III) in the samples, the increase in luminescence was not the result of lanthanide luminescence or its synonym columinescence. Thus, features set forth in claim 1 of the '744 patent are not present in the present invention, namely, in the present invention there is no requirement in the

present invention of "one energy transfer donor compound of yttrium or a 3-valent lanthanide element having atomic number 59-71, provided that the lanthanide element of said macrocycle compound and the lanthanide element of said energy transfer donor compound are not identical."

14. In view of the above, and as an expert in the field to which the present application pertains, I do not believe that the '744 patent discloses each and every element of the present invention. Further, I do not believe that the subject matter of the present invention is obvious in view of the '744 patent. In fact, the subject matter of the present application is taught away from in the '744 patent, and the present subject matter produces unexpected and surprising results.

15. I declare that all statements made herein of my own knowledge and are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the present application or any patent issued thereon.

Date: March 28, 2011


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